Amendments to the Claims:

This listing of claims replaces all prior versions, and listings, of claims in the application:

Listing of Claims:

1 to 5. (canceled)

6. (currently amended) A method of ~~treating an immunoregulatory abnormality~~ suppressing the immune system in a mammalian patient in need of such ~~treatment~~ immunosupression comprising administering to said patient a compound which is an agonist of the $S1P_1$/Edg1 receptor in an amount effective for ~~treating said immunoregulatory abnormality~~ suppressing the immune system, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the $S1P_3$/Edg3 receptor of at least 100 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the $S1P_3$/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay and wherein said compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 10 nM or less as evaluated by the ^{35}S-GTPγS binding assay,

wherein the ^{35}S-GTPγS binding assay is described as follows:

^{35}S-GTPγS Binding Assay

Functional coupling of S1P/Edg receptors to G proteins was measured in a ^{35}S-GTPγS binding assay; Membranes prepared as described in the Ligand Binding to Edg/S1P Receptors Assay (1-10 μg of membrane protein) were incubated in a 200 μl volume containing 20 mM HEPES pH 7.4, 100 mM NaCl, 10 mM $MgCl_2$, 5 μM GDP, 0.1% fatty acid-free BSA (Sigma, catalog A8806), various concentrations of sphingosine-1-phosphate, and 125 pM ^{35}S-GTPγS (NEN; specific activity 1250 Ci/mmol) in 96 well microtiter dishes; Binding was performed for 1 hour at room temperature with gentle mixing, and terminated by harvesting the membranes onto GF/B filter plates with a Packard Filtermate Universal Harvester; After drying the filter plates for 30 min, 40 μl of Microscint 20 was added to each well and binding was measured on a Wallac Microbeta Scintillation Counter;

Agonists and antagonists of S1P/Edg receptors can be discriminated in the ^{35}S-GTPγS binding assay; Compounds diluted in DMSO, methanol, or other solvent, were added to microtiter dishes to provide final assay concentrations of 0.01 nM to 10 μM; Membranes prepared from cells expressing S1P/Edg receptors were added, and binding to ^{35}S-GTPγS was performed as described; When assayed in the absence of the natural ligand or other known agonist, compounds that stimulate ^{35}S-GTPγS binding above the endogenous level were considered agonists, while compounds that inhibit the endogenous level of ^{35}S-GTPγS binding were considered inverse agonists; Antagonists were detected in a ^{35}S-GTPγS binding assay in the presence of a sub-maximal level of natural ligand or known S1P/Edg receptor agonist, where the compounds reduced the level of ^{35}S-GTPγS binding; Determination of the amount of binding in the presence of varying concentrations of compound was used to measure the potency of compounds as agonists, inverse agonists, or antagonists of S1P/Edg receptors; To evaluate agonists, percent stimulation over basal was calculated as binding in the presence of compound divided by binding in the absence of ligand, multiplied by 100; Dose response curves were plotted using a non-linear regression curve fitting program MRLCalc (Merck Research Laboratories), and EC_{50} values were defined to be the concentration of agonist required to give 50% of its own maximal stimulation; Selectivity of compounds for S1P/Edg receptors was determined by measuring the level of ^{35}S-GTPγS binding in the presence of compound using membranes prepared from cells transfected with each respective receptor;

and wherein the Ligand Binding to Edg/S1P Receptors Assay is described as follows:

Ligand Binding to Edg/S1P Receptors Assay

^{33}P-sphingosine-1-phosphate was synthesized enzymatically from γ^{33}P-ATP and sphingosine using a crude yeast extract with sphingosine kinase activity in a reaction mix containing 50 mM KH_2PO_4, 1 mM mercaptoethanol, 1 mM Na_3VO_4, 25 mM KF, 2 mM semicarbazide, 1 mM Na_2EDTA, 5 mM $MgCl_2$, 50 mM sphingosine, 0.1% TritonX-114, and 1 mCi γ^{33}P-ATP (NEN; specific activity 3000 Ci/mmol); Reaction products were extracted with butanol and ^{33}P-sphingosine-1-phosphate was purified by HPLC;

Cells expressing EDG/S1P receptors were harvested with enzyme-free dissociation solution (Specialty Media, Lavallette, NJ); They were washed once in cold PBS and suspended in binding assay buffer consisting of 50 mM HEPES-Na, pH 7.5, 5mM $MgCl_2$, 1mM $CaCl_2$, and 0.5% fatty acid-free BSA; ^{33}P-sphingosine-1-phosphate was sonicated with 0.1 nM

sphingosine-1-phosphate in binding assay buffer; 100 µl of the ligand mixture was added to 100 µl cells (1 x 10^6 cells/ml) in a 96 well microtiter dish; Binding was performed for 60 min at room temperature with gentle mixing; Cells were then collected onto GF/B filter plates with a Packard Filtermate Universal Harvester; After drying the filter plates for 30 min, 40 µl of Microscint 20 was added to each well and binding was measured on a Wallac Microbeta Scintillation Counter; Non-specific binding was defined as the amount of radioactivity remaining in the presence of 0.5 µM cold sphingosine-1-phosphate;

Alternatively, ligand binding assays were performed on membranes prepared from cells expressing Edg/S1P receptors; Cells were harvested with enzyme-free dissociation solution and washed once in cold PBS; Cells were disrupted by homogenization in ice cold 20 mM HEPES pH 7.4, 10 mM EDTA using a Kinematica polytron (setting 5, for 10 seconds); Homogenates were centrifuged at 48,000 x g for 15 min at 4°C and the pellet was suspended in 20 mM HEPES pH 7.4, 0.1 mM EDTA; Following a second centrifugation, the final pellet was suspended in 20 mM HEPES pH 7.4, 100 mM NaCl, 10 mM $MgCl_2$; Ligand binding assays were performed as described above, using 0.5 to 2 µg of membrane protein;

Agonists and antagonists of Edg/S1P receptors can be identified in the ^{33}P-sphingosine-1-phosphate binding assay; Compounds diluted in DMSO, methanol, or other solvent, were mixed with probe containing ^{33}P-sphingosine-1-phosphate and binding assay buffer in microtiter dishes; Membranes prepared from cells expressing Edg/S1P receptors were added, and binding to ^{33}P-sphingosine-1-phosphate was performed as described; Determination of the amount of binding in the presence of varying concentrations of compound and analysis of the data by non-linear regression software such as MRLCalc (Merck Research Laboratories) or PRISM (GraphPad Software) was used to measure the affinity of compounds for the receptor; Selectivity of compounds for Edg/S1P receptors was determined by measuring the level of ^{33}P-sphingosine-1-phosphate binding in the presence of the compound using membranes prepared from cells transfected with each respective receptor ($S1P_1$/Edg1, $S1P_3$/Edg3, $S1P_2$/Edg5, $S1P_4$/Edg6, $S1P_5$/Edg8).

7. (original) The method according to Claim 6 wherein the compound possesses an EC_{50} for binding to the $S1P_1$/Edg1 receptor of 1 nM or less as evaluated by the ^{35}S-GTPγS binding assay.

8. (original) The method according to Claim 6 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 200 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

9. (original) The method according to Claim 8 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 500 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

10. (original) The method according to Claim 9 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1P3/Edg3 receptor of at least 1000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1PR3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

11. (original) The method according to Claim 10 wherein the compound has a selectivity for the $S1P_1$/Edg1 receptor over the S1PR3/Edg3 receptor of at least 2000 fold as measured by the ratio of EC_{50} for the $S1P_1$/Edg1 receptor to the EC_{50} for the S1P3/Edg3 receptor as evaluated in the ^{35}S-GTPγS binding assay.

12 to 61. (canceled)